

STUDY TAGGING FILES SPECIFICATION

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Study Tagging Files Specification

Background

The testing conducted during step two for the eCTD indicated further definition was needed to provide for organization of files related to clinical and non-clinical studies. This definition should provide the information needed to organize files by study and various other aspects of the information. The method should allow for submissions of a study report in a single file or in multiple files. The method used for this should also have minimal impact on the implementation of the eCTD backbone, especially for those who wish not to use the added study definition.

This study definition for organizing study files can be used at every position in the eCTD that is intended for placement of study reports and study data. It can be used at the following CTD locations: Module 4- 4.2.1.1, 4.2.1.2, 4.2.1.3, 4.2.1.4, 4.2.2.1, 4.2.2.2, 4.2.2.3, 4.2.2.4, 4.2.2.5, 4.2.2.6, 4.2.2.7, 4.2.3.1, 4.2.3.2, 4.2.3.3.1, 4.2.3.3.2, 4.2.3.4.1, 4.2.3.4.2, 4.2.3.4.3, 4.2.3.5.1, 4.2.3.5.2, 4.2.3.5.3, 4.2.3.5.4, 4.2.3.6, 4.2.3.7.1, 4.2.3.7.2, 4.2.3.7.3, 4.2.3.7.4, 4.2.3.7.5, 4.2.3.7.6, 4.2.3.7.7; Module 5- 5.3.1.1, 5.3.1.2, 5.3.1.3, 5.3.1.4, 5.3.2.1, 5.3.2.2, 5.3.2.3, 5.3.3.1, 5.3.3.2, 5.3.3.3, 5.3.3.4, 5.3.3.5, 5.3.4.1, 5.3.4.2, 5.3.5.1, 5.3.5.2, 5.3.5.3, 5.3.5.4, 5.3.6, 5.3.7.

The additional study definition is provided by the applicant or sponsor in an XML instance controlled by a Document Type Definition (DTD). The name of the XML instance used in this narrative is the “Study Tagging File (STF) XML file”.

File Names, Directory Structure and eCTD leaf

For each study provided to the regulatory authority, you should provide a separate STF XML file. The name for the STF XML file should start with the term "stf-" followed by a term that clearly identifies the study and include ".xml" to complete the file name. The sponsors internal study identification number or alpha numeric can be adequate. If additional information is submitted to a study as new, replacement or amendment information, an additional STF XML file should be provided that contains information for only the new files being provided.

You can use the same directory structure for the study files as recommended in the eCTD Specification. The file or collection of files and the STF should be placed in the same directory separate from other independent studies. This includes files containing data and CRFs. A subdirectory structure can be used, but it is not specified here.

You should place a leaf element in the eCTD for each STF XML file. You should make sure that the leaf element for each STF XML file has a "version" attribute with a value of "STF Version 2.0". This will allow regulatory authorities to develop tools that either ignore or highlight the presence of the STF XML file.

If additional information is submitted to a study as new, replacement or amendment information, a new STF XML file should be provided. The new eCTD backbone file

should provide life cycle information regarding the STF XML file and the other files provided for the study. If an additional file is provided for a previously submitted study, the STF XML file's leaf operation attribute should have a value that is either "append" or "replace" depending on the applicant's intent. If a study is being removed from the application, the leaf operation attribute should have a value of "delete". In each of these examples the modified-file attribute should have a value that references the path and filename of the old STF XML file.

Example Study Report and STF XML File Lifecycle

A clinical study was performed under study identification AA012t. This was a double blind parallel study with an open label extension. When the double blind portion of the study was complete, the information was sent in the initial regulatory submission 0000. The Open Label portion of the study was completed later and the information was appended to the original study report as part of submission 0004. The applicant subsequently revised the study report and the original report was replaced in submission 0014. This example can be represented in the following table:

serial	Study Report file in eCTD backbone	STF XML Files in eCTD backbone
0000	studyaa012t.pdf ID="id12345" operation="new" modified-file=""	stf-aa012t.xml ID="id78690" operation="new" modified-file=""
0004	studyaa012t-1.pdf ID="id54321" operation="append" modified-file="..//0000/index.xml#id12345"	stf-aa012t-1.xml ID="id68690" operation="append" modified-file="..//0000/index.xml#id78690"
0014	studyaa012t-2.pdf ID="id12567" operation="replace" modified-file="..//0000/index.xml#id12345" operation="delete" modified-file="..//0004/index.xml#id54321"	stf-aa012t-2.xml ID="id86950" operation="replace" modified-file="..//0000/index.xml#id78690" operation="delete" modified-file="..//0004/index.xml#id68690"

Study Tagging File XML Discussion

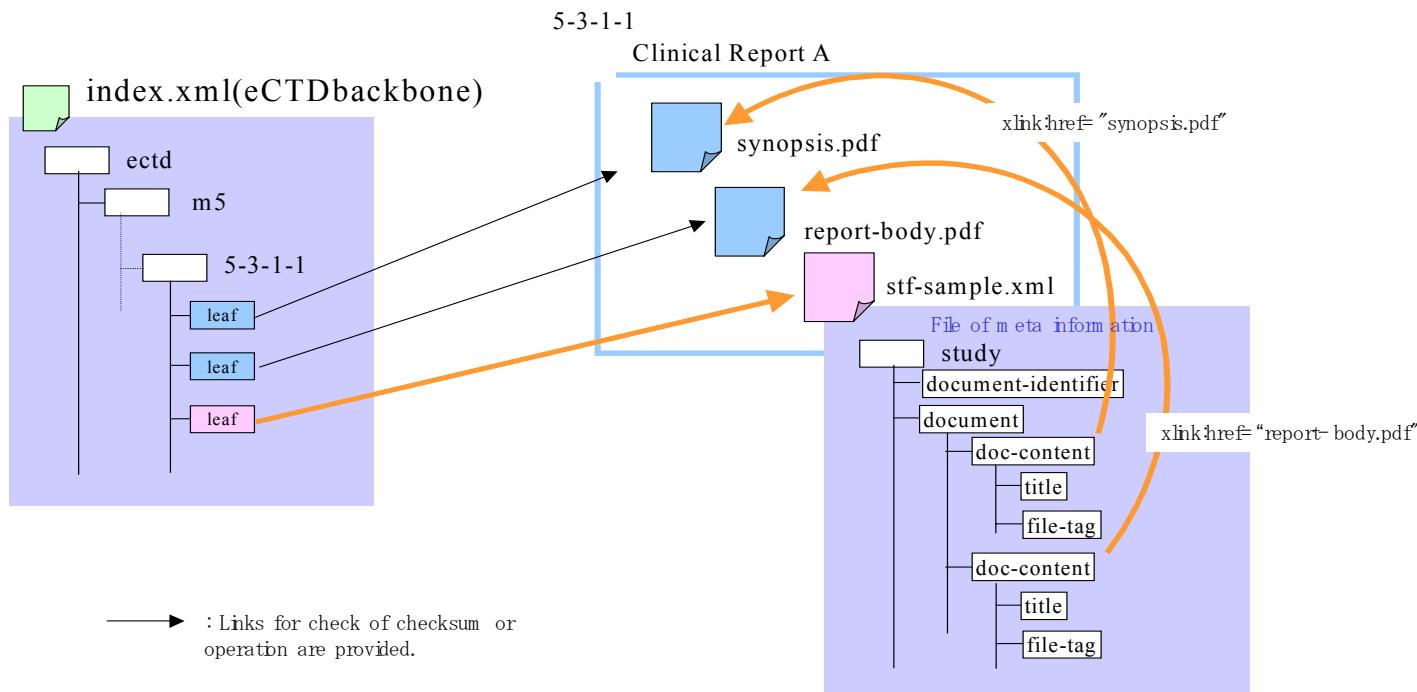
The name of the document type definition (DTD) that controls the organization of the STF XML file is "ich-stf.dtd". You should place a copy of the "ich-stf.dtd" file in the dtd folder so that its path and filename relative to the submission serial number is ".../util/dtd/ich-stf.dtd".

The name of the default stylesheet that controls the content of the STF is "ich-stf-stylesheet.xsl". You should place a copy of the stylesheet in the style folder so that its path and filename relative to the submission serial number is ".../util/style/ich-stf-stylesheet.xsl".

The STF XML file contains no leaf elements and replaces no leaf in the eCTD. The information in the STF XML file is associated with the study's file or files through the leaf elements that occur in the eCTD backbone. The STF XML file provides additional meta data about an eCTD leaf element that is not apparent in the eCTD. Information about the study is indicated according to the study title, study identification, subject species, route of administration and form of control used in the study. Information about an individual file for a study is provided as one or more content labels. The valid values for indicating species, route of administration, form of control and the file content labels can be restricted to a pick list of terms. The pick list can be provided in a stylesheet or schema referenced in the declaration section of the STF XML file. A default pick list for these terms is described later in this document. A default stylesheet that flags terms used that are not on the default pick-list is also described later in this document.

A graphical representation of the relationship between the eCTD leaf elements and the STF XML file is provided on the next page.

Approach of StudyReport DTD



STF XML File Specification

Declaration Section

The declaration section of the STF XML file contains information about the version of the XML standard being used (1.0) and the characters that are allowed in the file (UTF-8). It also contains reference to the stylesheet and to the document type definition (DTD). It also contains technical information about language, version, and name space declarations. An example of the declaration section is provided and it is based on the following information:

- An application, N12345, contains a study in Module 5 with an associated STF XML file. The applicant can place the STF XML files in a separate folder such as:

N12345\0002\m5\stffiles\..

or even

N12345\0002\m5\5311-ba-stud-rep\..

to keep the STF XML files near the associated study report files.

- The document type definition (DTD) is located in the specified location
- The default stylesheet is being used and is located in the specified location

Example XML

```
<?xml version="1.0" encoding="UTF-8"?>
<?xml-stylesheet type="text/xsl" href="../../util/style/ich-stf-stylesheet.xsl"?>
<!DOCTYPE ectd:study SYSTEM "../../util/dtd/ich-stf.dtd">
```

The declaration in your STF XML file can be different if the information about the location of the STF XML file, DTD or stylesheet changes.

ectd:study Element

This is the root element. It contains all the other elements in the STF XML file. The remaining elements are divided into two groups. The first group describes the study document as a whole whether it is a single file or a group of files. The second group describes each individual file for the study and attaches this description to the file's leaf element in the eCTD backbone file.

document-identifier Element

This element holds the group of elements that describes the study regardless of how many related files are provided for the study. The *title*, *doc-id*, and *category* elements provide data that describes the study.

***title* Element**

You should provide one *title* element for each STF XML file. The *title* element contains the full study title. The study title should not be abbreviated in this location.

***doc-id* Element**

You should provide one *doc-id* element for each STF XML file. This is the internal alphanumeric code used by the sponsor to unambiguously identify this study.

***category* Element**

You should place three *category* elements at the same level as the *title* and *doc-id* elements. They should each have two attributes named *name* and *info-type*. For each of these, the value of the *info-type* attribute specified by the default stylesheet is "ich". The regulatory body receiving the information may specify a different value for the *info-type* attribute. The value of the *name* attributes should be selected from "species", "route-of-admin" or "type-of-control". The purpose of the *category* element depends on the value of the *name* attribute as follows:

When you give the *name* attribute a value of "species", the content of the *category* element indicates the species that is the subject of the study. The content should be limited to the values in the table below this text. If a study includes more than one species, an additional *category* element should be provided with a *name* attribute value describing the additional species.

When you give the *name* attribute the value of "route-of-admin", the content of the *category* element indicates the route of administration used for the study. The content should be limited to the values in the table below this text. If a study includes more than one route of administration, multiple *category* elements can be provided with *name* attribute values of "route-of-admin" to indicate additional routes of administration.

When you give the *name* attribute the value of "type-of-control" the content of the *category* element indicates the control used for the study (if any). The content should be limited to the values in the table below this text. If a study includes more than one control, multiple *category* elements can be provided with *name* attribute values of "type-of-control". Each can be used to indicate a different type of study control.

The content for the *category* elements should be selected from the values that are defined below. Using the default stylesheet, the specified content for the *category* element depends on the *category* element's *name* attribute value. The table below shows the specified content choices for the *category* element for each *name* attribute value when using the default stylesheet:

Category Element Attributes and Values	values defined in stylesheet for "category" element content choices
---	--

Category Element Attributes and Values	values defined in stylesheet for "category" element content choices
name="species" info-type="ich"	mouse
	rat
	other-rodent
	rabbit
	dog
	nonhuman-primate
	other-nonrodent-mammal
	nonmammal
	human
Name="route-of-admin" Info-type="ich"	oral
	intravenous
	intramuscular
	intraperitoneal
	subcutaneous
	inhalation
	topical
Name="type-of-control" Info-type="ich"	placebo
	No-treatment-control
	dose-response-without-placebo
	active-control-without-placebo
	external-control

Changes to the default stylesheet, attribute, attribute values and categories will be managed by the ICH Implementation Working Group eCTD Change Control Board.

Example XML

An example of the study elements is provided that indicates a bioequivalence study (species="human") conducted with an oral route of administration (route-of-

admin="oral") with dose-response-without-placebo (type-of-control="dose-response-without-placebo"):

```
<title>Study Report for Bioavailability</title>
<doc-id>ich-abc123xyz789</doc-id>
<category name="species" info-type="ich">human</category>
<category name="route-of-admin" info-type="ich">oral</category>
<category name="type-of-control"
          info-type="ich">dose-response-without-placebo
</category>
```

document Elements

The DTD contains the element *document* which STF XML files use for organising the components of the file. The *document* element may contain any mix of *doc-content* and *content-block* elements. For discussion and description only the *document* element can be viewed as two subtypes: SINGLE using “*doc-content*” and MULTIPLE using *content-block* tag sections. A STF XML file may be composed of only SINGLE tag sections, MULTIPLE tag sections or a combination of both sections.

doc-content element use in SINGLE tag section

The SINGLE tag section is prepared with the *doc-content* element, which contains the *title*, *property*, and *file-tag* elements plus the attribute *xlink:href* for the file on the eCTD backbone. An optional *property* element is provided for inclusion and filtering data that may be required by another regional regulatory authority. The *file-tag* contains the elements *name* and *info-type*.

When preparing a STF XML file containing a SINGLE tag section you should place the full title of the study being described by the STF XML in the *title* element.

The *property* element may be needed by some regional authorities. For submissions to the US regulatory authority, Food and Drug Administration (FDA), you should include a *property* element when the relative path and file name is provided in the *xlink:href*. The *property* element should have the *name* attribute of “leaf-id” and the *info-type* attribute of “fda”. The *property* value should be the ID value from the index.xml file for the report file the STF XML file is describing. For example, the backbone includes a legacy study report in a file called legstudy.pdf with index.xml ID of id1002. The *property* element describing this should look like:

```
<property name="leaf-id" info-type="fda">..//0005/index.xml#id1002</property>
```

and would be contained in the *doc-content* element. If the file the STF XML is referring to is in a previous submission (e.g., serial 0002), the value for the *property* element should be entered as:

```
<property name="leaf-id" info-type="fda">..//0002/index.xml#id1235</property>
```

Note that all references must be relative to the location of the STF XML file in the submission.

The text value of the *file-tag* element's *name* attribute indicates the subject matter that is in the file being described. The value of the *file-tag name* attribute should be selected from the valid values that are defined by the regulatory body receiving the information. If the file being described contains subject matter from more than one of the valid *name* attribute values, you should provide multiple *file-tag* elements each with a single subject matter value in its *name* attribute. The *info-type* attribute provides information about the list of values from which the *name* attribute's value was selected. A regulatory body receiving the information can specify additional *file-tag name* attribute values that are specified with a different *info-type* attribute value. The default stylesheet specifies an *info-type* attribute value of "ich-e3". The table below shows the specified *name* attribute values for the *file-tag* element specified by the default stylesheet correlated with a description of the file's content:

"file-tag" Element Attribute Values **	Content of File
name="legacy-study-report" info-type="ich-e3"	File contains the complete study report.
name="synopsis" info-type="ich-e3"	File contains Study Report Synopsis (E3 2)
name="study-report-body" info-type="ich-e3"	File contains Study Report Body (E3 1, 3 to 15)
name="protocol-or-amendment" info-type="ich-e3"	File contains Protocol and/or amendments (E3 16.1.1)
name="sample-case-report-form" info-type="ich-e3"	File contains sample CRF (E3 16.1.2)
name="iec-erb-consent-form-list" info-type="ich-e3"	File contains IEC and ERB and Consent Form Listings (E3 16.1.3)

"file-tag" Element Attribute Values **	Content of File
name="list-description-investigator-site" info-type="ich-e3"	File contains List and Description of Investigator Sites (E3 16.1.4)
name="signatures-investigators" info-type="ich-e3"	File contains Signatures of principal or coordinating investigator(s) or sponsor's responsible medical officer (E3 16.1.5)
name="list-patients-with-batches" info-type="ich-e3"	File contains Listing of patients receiving test drug(s) from specified batch (E3 16.1.6)
name="randomisations-scheme" info-type="ich-e3"	File contains Randomisations Scheme (E3 16.1.7)
name="audit-certificates-report" info-type="ich-e3"	File contains Audit Certificates (E3 16.1.8)
name="statistical-methods-interim-analysis-plan" info-type="ich-e3"	File contains Documentation of statistical methods and interim analysis plans (E3 16.1.9)
name="inter-laboratory-standardisation-methods-quality-assurance" info-type="ich-e3"	File contains Documentation of Inter-laboratory Standardization Methods and Quality Assurance (16.1.10)
name="publications-based-on-study" info-type="ich-e3"	File contains Publications Based on the Study (E3 16.1.11)
name="publications-referenced-in-report" info-type="ich-e3"	File contains Publications Referenced in the Study Report (E3 16.1.12)
name="discontinued-patients" info-type="ich-e3"	File contains Discontinued Patients Listing (16.2.1)
name="protocol-deviations" info-type="ich-e3"	File contains Protocol Deviation Listing (E3 16.2.2)
name="patients-excluded-from-efficacy-analysis" info-type="ich-e3"	File contains Patients Excluded from Efficacy Analysis Listing (E3 16.2.3)

"file-tag" Element Attribute Values **	Content of File
<code>name="demographic-data"</code> <code>info-type="ich-e3"</code>	File contains Demographic Data Listing (E3 16.2.4)
<code>name="compliance-and-drug-concentration-data"</code> <code>info-type="ich-e3"</code>	File contains Compliance and/or Drug Concentration Data Listing (16.2.5)
<code>name="individual-efficacy-response-data"</code> <code>info-type="ich-e3"</code>	File contains Individual Efficacy Response Data Listing (E3 16.2.6)
<code>name="adverse-event-listings"</code> <code>info-type="ich-e3"</code>	File contains Adverse Event Listings Listing (E3 16.2.7)
<code>name="listing-individual-laboratory-measurements-by-patient"</code> <code>info-type="ich-e3"</code>	File contains Individual Laboratory Measurements Listed by Patient (E3 16.2.8)
<code>name="case-report-forms"</code> <code>info-type="ich-e3"</code>	File contains CRF for an individual subject (E3 16.3). You should also provide a "property" element, described below, with its "name" attribute = "site-identifier" and its value the site identification where the study was performed.
<code>name="individual-subject-data-listing"</code> <code>info-type="ich-e3"</code>	File contains Individual Patient or Subject Data Listings (E3 16.4).
<code>name="nonclinical-data"</code> <code>info-type="ich-e3"</code>	Content of element is for additional leaf label information for preclinical or nonclinical studies. Place text for a single term as contents of this element. There is no limit to the number of times this element can occur.
** These values should also be used in MULTIPLE tag sections (e.g., CRFS)	

content-block use in MULTIPLE tag sections

When multiple tags could be used for the same backbone file or when multiple files are related to a single study the MULTIPLE tag file form of the *document* element can be used. The MULTIPLE tag file uses the *content-block* element to group the related tags or files under a common heading.

The *content-block* is created with *block-title*, *property*, *doc-content*, *file-tag*, and *content-block* elements and can be used for hierarchical organisation of file tags or files. The value provided for the *block-title* is used to group the related file tags or files when displayed by the stylesheet. When used as an attribute of *content-block* the *title* attribute of the *doc-content* element may not be needed (e.g., when including relative paths for the case report forms related to a specific site).

For submissions to the US regulatory authority, Food and Drug Administration (FDA), you can use additional *file-tag* element *name* attribute values. When you submit study information with the appropriate file content for these additional tags, you should provide the *file-tag* element's *info-type* attribute a value of "fda". The table below shows the specified *name* attribute values for the *file-tag* element specified when using the additional values for submission to the US regional regulatory authority:

"file-tag" Element Attribute Values	Content of File
<code>name="data-tabulation-dataset" info-type="fda"</code>	File contains datasets for the Data tabulation
<code>name="data-tabulation-data- definition" info-type="fda"</code>	File contains data definitions for the data tabulation
<code>name="data-listing-dataset" info-type="fda"</code>	File contains datasets for data listing datasets
<code>name="data-listing-data-definition" info-type="fda"</code>	File contains data definitions for data listing
<code>name="analysis-dataset" info-type="fda"</code>	File contains datasets for analysis datasets
<code>name="analysis-program" info-type="fda"</code>	File contains analysis programs for analysis datasets
<code>name="analysis-data-definition" info-type="fda"</code>	File contains data definitions for analysis datasets
<code>name="safety-report" info-type="fda"</code>	File contains investigational new drug application (IND) safety reports
<code>name="subject-profile" info-type="fda"</code>	File contains an individual subject profiles

<code>name="annotated-crf"</code> <code>info-type="fda"</code>	File contains an annotated case report form (CRF)
---	---

For submissions to the US regulatory authority, Food and Drug Administration (FDA), you can use an extension to the *file-tag* element called the *property* element. When you submit study information with the appropriate file you should provide a *property* element for additional information about the site where the study was conducted. When you use a *file-tag* element with the *name* attribute value of "subject-profile" or "case-report-forms" for submission to the FDA, you should include the *property* element. The *property* element's *info-type* attribute value should be "fda" and the *name* attribute value should be "site-identifier". The content of the *property* element should be text that identifies the site relevant to the file.

Example XML

A sponsor is submitting a study titled "Wonderdrug Phase III Clinical Study Report for AA-S107t" performed under their in-house identification "AA-S107t". The study involved patients that received Wonderdrug orally. The study is presented following the E3 granularity specification. In this example, the synopsis is one file named "synopsis.pdf" that contains a report titled "Wonderdrug Study AA-S107t Synopsis". The body of the clinical study report is in a file named "report-body.pdf" and it contains the report titled "Wonderdrug Study AA-S107t Clinical Study Report Body". Case report forms are provided for patients at study sites 111 and 333. The corresponding STF XML file is named "STF-AA-S107t.XML" and follows:

```
<?xml version="1.0" encoding="UTF-8"?>
<?xml-stylesheet type="text/xsl" href="../util/style/ich-stf-stylesheet.xsl"?>
<!DOCTYPE ectd:study SYSTEM "../util/dtd/ich-stf.dtd">
<ectd:study xmlns:ectd="http://www.ich.org/ectd" xml:lang="en" dtd-version="2.0"
xmlns:xlink="http://www.w3c.org/1999/xlink">
  <document-identifier>
    <title>Wonderdrug Phase III Clinical Study Report for AA-S107t</title>
    <doc-id>AA-S107t</doc-id>
    <category name="species" info-type="ich">human</category>
    <category name="route-of-admin" info-type="ich">oral</category>
    <category name="type-of-control" info-type="ich"> placebo</category>
  </document-identifier>
  <document>
    <doc-content xlink:href="synopsis.pdf">
      <title>Wonderdrug Study AA-S107t Synopsis</title>
      <property name="leaf-id" info-type="fda">..0005/index.xml#id1020</property>
      <file-tag name="synopsis" info-type="ich-e3"/>
    </doc-content>
    <doc-content xlink:href="report-body.pdf">
      <title>Wonderdrug Study AA-S107t Clinical Study Report Body</title>
      <property name="leaf-id" info-type="fda">..0005/index.xml#id1021</property>
      <file-tag name="study-report-body" info-type="ich-e3"/>
    </doc-content>
    <content-block>
      <block-title>Case Reports for site 111</block-title>
      <doc-content xlink:href="">
```

```

<file-tag name="case-report-forms" info-type="ich-e3">
    <property name="site-identifier" info-type="fda">111</property>
</file-tag>
</doc-content>
<doc-content xlink:href="crf-for-patient-0001.pdf">
    <property name="leaf-id" info-type="fda">..0005/index.xml#id1022</property>
</doc-content>
<doc-content xlink:href="crf-for-patient-0002.pdf">
    <property name="leaf-id" info-type="fda">..0005/index.xml#id1023</property>
</doc-content>
<doc-content xlink:href="crf-for-patient-nnnn.pdf">
    <property name="leaf-id" info-type="fda">..0005/index.xml#id1024</property>
</doc-content>
</content-block>
<content-block>
    <block-title>Case Reports for study site 333</block-title>
<doc-content xlink:href="">
    <file-tag name="case-report-forms" info-type="ich-e3">
        <property name="site-identifier" info-type="fda">333</property>
    </file-tag>
</doc-content>
<doc-content xlink:href="crf-for-patient-0101.pdf">
    <property name="leaf-id" info-type="fda">..0005/index.xml#id1025</property>
</doc-content>
<doc-content xlink:href="crf-for-patient-0102.pdf">
    <property name="leaf-id" info-type="fda">..0005/index.xml#id1026</property>
</doc-content>
<doc-content xlink:href="crf-for-patient-zzzz.pdf">
    <property name="leaf-id" info-type="fda">..0005/index.xml#id1027</property>
</doc-content>
</content-block>
</document>
</ectd:study>

```

Additional Example XML

This is a hypothetical case intended to utilize all of the ich-stf.dtd tags. The final section of the example demonstrates the validation performed and presented by the default stylesheet.

A sponsor is submitting a study titled “Study Report for Bioavailability” performed under their in-house identification “BA-S107t”. The study involved human test subjects receiving Wonderdrug to measure dose response in a “dose-response-without-placebo” study. The study is presented following E3 granularity and has one file named “synopsis.pdf” containing a report titled “Bioavailability Synopsis Update” and a file named “report-body.pdf” containing a report titled “Bioavailability Report Body”. In addition case report forms were provided for study subjects at study sites 111 and 333. Also additional documentation relating to the study is provided in a combined report. This study will be submitted to both the Japan and US regulatory authorities and contains some additional test results for the Japan regulatory authority. A STF XML file named “stf-ba-s107t.xml” can be prepared as follows:

```
<?xmlstylesheet type="text/xsl" href="..util/style/ich-stf-stylesheet.xsl"?>
```

```

<!DOCTYPE ectd:study SYSTEM "..//util/dtd/ich-stf.dtd">
<ectd:study xmlns:ectd="http://www.ich.org/ectd" xml:lang="en" dtd-version="2.0"
xmlns:xlink="http://www.w3c.org/1999/xlink">
  <document-identifier>
    <title>Study Report for Bioavailablility</title>
    <doc-id>BA-S107t</doc-id>
    <category name="species" info-type="ich">human</category>
    <category name="route-of-admin" info-type="ich">oral</category>
    <category name="type-of-control" info-type="ich">dose-response-without-
placebo</category>
  </document-identifier>
  <document>
    <doc-content xlink:href="legacy-synopsis.pdf">
      <title>Legacy-Study Report BA-S107t </title>
      <property name="leaf-id" info-type="fda">..//0005/index.xml#id1020</property>
      <file-tag name="legacy-study-report" info-type="ich-e3"/>
    </doc-content>
    <doc-content xlink:href="synopsis.pdf">
      <title>Bioavailability Synopsis</title>
      <property name="leaf-id" info-type="fda">..//0005/index.xml#id1021</property>
      <file-tag name="synopsis" info-type="ich-e3"/>
    </doc-content>
    <doc-content xlink:href="report-body.pdf">
      <title>Bioavailability Report Body</title>
      <property name="leaf-id" info-type="fda">..//0005/index.xml#id1123</property>
      <file-tag name="study-report-body" info-type="ich-e3"/>
    </doc-content>
    <content-block>
      <block-title>appendix</block-title>
      <property name="test" info-type="jpma">value</property>
      <property name="test2" info-type="mhlw">value2</property>
      <doc-content xlink:href="combined-information-file.pdf">
        <title>Bioavailability Combined File</title>
        <property name="test7" info-type="jpma">value5</property>
        <property name="leaf-id" info-type="fda">..//0005/index.xml#id1124</property>
        <file-tag info-type="ich-e3" name="protocol-or-amendment"/>
        <file-tag name="sample-case-report-form" info-type="ich-e3"/>
        <file-tag name="iec-erb-consent-form-list" info-type="ich-e3"/>
        <file-tag name="list-description-investigator-site" info-type="ich-e3"/>
        <file-tag name="list-patients-with-batches" info-type="ich-e3"/>
        <file-tag name="randomisations-scheme" info-type="ich-e3"/>
        <file-tag name="audit-certificates-report" info-type="ich-e3"/>
        <file-tag name="statistical-methods-interim-analysis-plan" info-type="ich-e3"/>
        <file-tag name="inter-laboratory-standardization-methods-quality-assurance" info-
type="ich-e3"/>
        <file-tag name="publications-based-on-study" info-type="ich-e3"/>
        <file-tag name="publications-referenced-in-report" info-type="ich-e3"/>
        <file-tag name="discontinued-patients" info-type="ich-e3"/>
        <file-tag name="protocol-deviations" info-type="ich-e3"/>
        <file-tag name="patients-excluded-from-efficacy-analysis" info-type="ich-e3"/>
        <file-tag name="demographic-data" info-type="ich-e3"/>
        <file-tag name="compliance-and-drug-concentration-data" info-type="ich-e3"/>
        <file-tag name="individual-efficacy-response-data" info-type="ich-e3"/>
        <file-tag name="adverse-event-listings" info-type="ich-e3"/>
        <file-tag name="listing-individual-laboratory-measurements-by-patient" info-
type="ich-e3"/>
      </doc-content>
    </content-block>
  </document>
</ectd:study>

```

```

    </doc-content>
    <content-block>
        <block-title>Case Reports for first site</block-title>
        <file-tag name="case-report-forms" info-type="ich-e3">
            <property name="site-identifier" info-type="fda">111</property>
        </file-tag>
        <doc-content xlink:href="crf-for-patient-0001.pdf">
            <property name="leaf-id" info-type="fda">..0005/index.xml#id1125</property>
        </doc-content>
        <doc-content xlink:href="crf-for-patient-0002.pdf">
            <property name="leaf-id" info-type="fda">..0005/index.xml#id1126</property>
        </doc-content>
        <doc-content xlink:href="crf-for-patient-nnnn.pdf">
            <property name="leaf-id" info-type="fda">..0005/index.xml#id1127</property>
        </doc-content>
    </content-block>
    <content-block>
        <block-title>Next study site</block-title>
        <file-tag name="case-report-forms" info-type="ich-e3">
            <property name="site-identifier" info-type="fda">333</property>
        </file-tag>
        <doc-content xlink:href="crf-for-patient-0101.pdf">
            <property name="leaf-id" info-type="fda">..0005/index.xml#id2127</property>
        </doc-content>
        <doc-content xlink:href="crf-for-patient-0102.pdf">
            <property name="leaf-id" info-type="fda">..0005/index.xml#id2128</property>
        </doc-content>
        <doc-content xlink:href="crf-for-patient-zzzz.pdf">
            <property name="leaf-id" info-type="fda">..0005/index.xml#id2129</property>
        </doc-content>
    </content-block>
</content-block>
<content-block>
    <block-title>Stylesheet validation example</block-title>
    <doc-content xlink:href="stf-validation-example.xml">
        <title>Bioavailability Data (stf with errors)</title>
        <property name="leaf-id" info-type="fda">..0005/index.xml#id3120</property>
        <file-tag name="subject-profile" info-type="fda">
            <property name="site-identifier" info-type="fda">222</property>
        </file-tag>
    </doc-content>
</content-block>
</document>
</ectd:study>

```

Document Type Definition (DTD)

The content and organisation of the STF is described in the text of this document above this point. The machine-readable instructions for the organization of the STF are provided in the form of a Document Type Definition (DTD). If there is a difference

between the text description and the DTD, the DTD will prevail. Regardless of the regulatory body receiving the submission, the STF should follow the organization rules in the DTD. A copy of the DTD is provided:

```
<!-- ICH Study Tagging File (ich-stf.dtd) -->
<!-- version 2-0 -->
<!-- For every study in the eCTD backbone there should be an
XML Study Tagging File that follows this DTD.
If two studies are contained in the same element on the backbone,
there should be an XML Study Tagging File for each.-->
<!ELEMENT ectd:study (document-identifier, document)>
<!ATTLIST ectd:study
  xmlns:ectd CDATA #FIXED "http://www.ich.org/ectd"
  xmlns:xlink CDATA #FIXED "http://www.w3c.org/1999/xlink"
  xml:lang CDATA #IMPLIED
  dtd-version CDATA #FIXED "2.0"
>
<!ELEMENT document-identifier (title, doc-id, category*)>
<!--
=====
document identifier
The following defines the study metadata that a review tool will use to
display/filter studies
  title      The full title of the report as on the title page of the report
  doc-id     The unambiguous code used by the sponsor to track the study.

=====
-->
<!--The following identifies the document(study) by title and doc-id alpha-
numeric-->
<!ELEMENT title (#PCDATA)>
<!ELEMENT doc-id (#PCDATA)>
<!--
=====
The category element defines high level characteristics/parameters of the study.
```

Each category has a content value and has the attributes: name and info-type. The value in the info-type will allow a stylesheet to ignore or display the named characteristic/parameter.

name:	identifies the characteristic/parameter class
info-type:	used to indicate related characteristics/parameters which can filter category for display or ignore
[category]	the specific value for the named characteristic/parameter class

```
=====
-->
<!ELEMENT category (#PCDATA)>
<!ATTLIST category
  name CDATA #REQUIRED
  info-type CDATA #REQUIRED
>
<!--
=====
document
```

This is a container for providing tagging information described as SINGLE or MULTIPLE (to facilitate description only) tags per file. SINGLE files are provided using the doc-content container described below. MULTIPLE tag files are provided using the content-block container which includes the doc-content container as an attribute.

SINGLE tag file use doc-content described as:

xlink:href: the relative path to the file

title: the full title of the study report as on the title page of the report which will be displayed by the review tool

property: an additional characteristic/parameter that may be required regionally to further describe a file-tag with the following attributes

name: describes the additional characteristic/parameter which may be needed regionally

info-type: attribute value is used to indicate related characteristics/parameters which can be used to filter the name attribute for display or to ignore the item if not required regionally

file-tag: a container with name and info-type attributes.

name: the list of valid values for the name is controlled by the ICH default stylesheet and by regional schemas, guidance or stylesheets that may be needed regionally. The name attribute holds the specific tag to be associated with the file.

info-type: attribute value is used to indicate related characteristics/parameters which can be used to filter the name attribute for display or to ignore the item if not required regionally

MULTIPLE tags per file use content-block described as:

block-title:	Used by the stylesheet as a section header for related items.
property:	Same as described in SINGLE
file-tag:	Same as described above
doc-content:	Same as described in SINGLE
content-block:	Provides for a hierarchical submission of related meta data.

```
=====
-->
<!ELEMENT document ((doc-content | content-block)*)>
<!ELEMENT doc-content (title?, property*, file-tag*)>
<!ATTLIST doc-content
  xlink:href CDATA #IMPLIED
  xlink:type CDATA #FIXED "simple"

>
<!ELEMENT content-block (block-title, property*, file-tag*, (doc-content | content-block)*)>
<!ELEMENT block-title (#PCDATA)>
<!ELEMENT file-tag (property*)>
<!ATTLIST file-tag
  name CDATA #REQUIRED
  info-type CDATA #REQUIRED
>
<!ELEMENT property (#PCDATA)>
<!ATTLIST property
  name CDATA #REQUIRED
  info-type CDATA #REQUIRED
>
```

Default Stylesheet

The content and organisation of the STF is described in the text of this document above this point. The machine-readable content of the STF is controlled by the default stylesheet. Different controls for the STF content can be provided by the regulatory body receiving the submission. Regardless of these additional controls, the STF organization should still be controlled by the DTD described in the previous section. A copy of the default stylesheet is provided:

```
<?xml version="1.0" encoding="UTF-8"?>
<!-- ICH STF Stylesheet (ich-stf-stylesheet.xsl) -->
<!-- version 2-0 -->
```

```

<xsl:stylesheet version="1.0" xmlns:xsl="http://www.w3.org/1999/XSL/Transform"
    xmlns:fo="http://www.w3.org/1999/XSL/Format"
    xmlns:xlink="http://www.w3c.org/1999/xlink"
    xmlns:internal="http://www.ich.org"
    xmlns:ectd="http://www.ich.org">
    <!-- This section provides the vocabulary for controlling content of some elements and
attribute values according
to info-type values -->
    <!--File tagging Vocabulary section-->
    <internal:vocabulary4leaf-labels-file-tag>
        <ich-e3>
            <item>legacy-study-report</item>
            <item>synopsis</item>
            <item>study-report-body</item>
            <item>protocol-or-amendment</item>
            <item>sample-case-report-form</item>
            <item>iec-erb-consent-form-list</item>
            <item>list-description-investigator-site</item>
            <item>signatures-investigators</item>
            <item>list-patients-with-batches</item>
            <item>randomisations-scheme</item>
            <item>audit-certificates-report</item>
            <item>statistical-methods-interim-analysis-plan</item>
            <item>inter-laboratory-standardization-methods-quality-assurance</item>
            <item>publications-based-on-study</item>
            <item>publications-referenced-in-report</item>
            <item>discontinued-patients</item>
            <item>protocol-deviations</item>
            <item>patients-excluded-from-efficacy-analysis</item>
            <item>demographic-data</item>
            <item>compliance-and-drug-concentration-data</item>
            <item>individual-efficacy-response-data</item>
            <item>adverse-event-listings</item>
            <item>listing-individual-laboratory-measurements-by-patient</item>
            <item>case-report-forms</item>
            <item>individual-subject-data-listing</item>
            <item>nonclinical-data</item>
        </ich-e3>
        <fda>
            <fda-data>
                <item>data-tabulation-dataset</item>
                <item>data-tabulation-data-definition</item>
                <item>data-listing-dataset</item>
                <item>data-listing-data-definition</item>
                <item>analysis-dataset</item>
                <item>analysis-program</item>
                <item>analysis-data-definition</item>
                <item>safety-report</item>
                <item>subject-profile</item>
                <item>annotated-crf</item>
            </fda-data>
            <fda-site>
                <item>site-identifier</item>
            </fda-site>
        </fda>
    </internal:vocabulary4leaf-labels-file-tag>

```

```

<!--Study properties Vocabulary section-->
<internal:vocabulary4study-category>
    <ich>
        <study-category-names>
            <item>species</item>
            <item>route-of-admin</item>
            <item>type-of-control</item>
        </study-category-names>
        <species>
            <item>mouse</item>
            <item>rat</item>
            <item>rabbit</item>
            <item>other-rodent</item>
            <item>dog</item>
            <item>nonhuman-primate</item>
            <item>other-nonrodent-mammal</item>
            <item>nonmammal</item>
            <item>human</item>
        </species>
        <type-of-control>
            <item>placebo</item>
            <item>no-treatment-control</item>
            <item>dose-response-without-placebo</item>
            <item>active-control-without-placebo</item>
            <item>external-control </item>
        </type-of-control>
        <route-of-admin>
            <item>oral</item>
            <item>intravenous</item>
            <item>intramuscular</item>
            <item>intraperitoneal</item>
            <item>subcutaneous</item>
            <item>inhalation</item>
            <item>topical</item>
        </route-of-admin>
    </ich>
</internal:vocabulary4study-category>
<!--The following is the data presentation section-->
<xsl:template match="/">
    <html xmlns="http://www.w3.org/1999/xhtml" xml:lang="en" lang="en">
        <head>
            <title>Study Tagging File (STF)</title>
        </head>
        <body>
            <h1>Study Files' Content Infomation</h1>
            <!-- The following table provides the study properties-->
            <table frame="hsides">
                <tr>
                    <th width="20%">Category</th>
                    <th width="80%" align="left">Category Value</th>
                </tr>
                <tr>
                    <xsl:for-each select="descendant::document-identifier/title">
                        <td>
                            Study Title:
                        </td>
                    </xsl:for-each>
                </tr>
            </table>
        </body>
    </html>

```

```

        <td>
            <xsl:value-of select=". "/>
        </td>
    </xsl:for-each>
</tr>
<tr>
    <td>
        Doc ID:
    </td>
    <td>
        <xsl:value-of select="descendant::document-identifier/doc-id"/>
    </td>
</tr>
<!--The following retrieves each property element with the info-type value of ich
--&gt;
&lt;xsl:for-each select="descendant::category[@info-type='ich']"&gt;
    &lt;!--The following is an error check that the name of the property is on the
    "ich" list and if not, provides a warning for both the property name and its
    content--&gt;
    &lt;xsl:choose&gt;
        &lt;xsl:when
test="@name=document('/')/xsl:stylesheet/internal:vocabulary4study-category/ich/study-category-
names/item"/&gt;
            &lt;xsl:otherwise&gt;
                &lt;tr&gt;
                    &lt;td&gt;
                        &lt;xsl:value-of select="@name"/&gt;-
                        (&lt;xsl:value-of select="@info-type"/&gt;)&lt;br/&gt;
                        &lt;font color="red"&gt;"&lt;xsl:value-of select="@name"/&gt;"-Not an
"&lt;xsl:value-of select="@info-type"/&gt;" List!&lt;/font&gt;
                    &lt;/td&gt;
                    &lt;td&gt;
                        &lt;xsl:value-of select=". "/&gt;
                        &lt;br/&gt;
                        &lt;font color="red"&gt;"&lt;xsl:value-of select=". "/&gt;"- Not Validated!
Because: No "&lt;xsl:value-of select="@info-type"/&gt;"&lt;br/&gt;
List For: "&lt;xsl:value-of select="@name"/&gt;"!&lt;/font&gt;
                    &lt;/td&gt;
                &lt;/tr&gt;
            &lt;/xsl:otherwise&gt;
        &lt;/xsl:choose&gt;
    &lt;/xsl:for-each&gt;
<!--The following three "for-each" loops retrieve the category elements according
to their name attribute value--&gt;
&lt;xsl:for-each select="descendant::category[@name='species']"&gt;
    &lt;tr&gt;
        &lt;td&gt;
            &lt;xsl:value-of select="@name"/&gt;-(&lt;xsl:value-of select="@info-
type"/&gt;)&lt;/td&gt;
        &lt;td&gt;
            &lt;xsl:value-of select=". "/&gt;
            &lt;br/&gt;
            &lt;!--The following is the error check for the list of species values in the
            ich list and if not, provides a warning--&gt;
            &lt;xsl:choose&gt;
</pre>

```

```

        <xsl:when
test=".=document("")/xsl:stylesheet/internal:vocabulary4study-category/ich/species/item"/>
        <xsl:otherwise>
            <font color="red">"<xsl:value-of select="."/>"- NOT on
List</font>
            </xsl:otherwise>
        </xsl:choose>
    </td>
</tr>
</xsl:for-each>
<xsl:for-each select="descendant::category[@name='route-of-admin']">
    <tr>
        <td>
            <xsl:value-of select="@name"/> -(<xsl:value-of select="@info-
type"/>)</td>
        <td>
            <xsl:value-of select="."/>
            <!--The following is the error check for the list of route-of-admin values
in the ich list if not, provides a warning-->
            <xsl:choose>
                <xsl:when
test=".=document("")/xsl:stylesheet/internal:vocabulary4study-category/ich/route-of-admin/item"/>
                    <xsl:otherwise>
                        <br/>
                        <font color="red">"<xsl:value-of select="."/>"- NOT on
List!</font>
                        </xsl:otherwise>
                    </xsl:choose>
                </td>
            </tr>
        </xsl:for-each>
        <xsl:for-each select="descendant::category[@name='type-of-control']">
            <tr>
                <td>
                    <xsl:value-of select="@name"/>(<xsl:value-of select="@info-
type"/>)</td>
                <td>
                    <xsl:value-of select="."/>
                    <br/>
                    <!--The following is the error check for the list of type-of-control values
in the ich list if not, provides a warning-->
                    <xsl:choose>
                        <xsl:when
test=".=document("")/xsl:stylesheet/internal:vocabulary4study-category/ich/type-of-control/item"/>
                            <xsl:otherwise>
                                <font color="red" face="bold">"<xsl:value-of select="."/>"- NOT
on "<xsl:value-of select="@info-type"/>" List!</font>
                            </xsl:otherwise>
                        </xsl:choose>
                    </td>
                </tr>
            </xsl:for-each>
        </table>
        <!--The following table lists the file tags and other properties for document-->
        <xsl:apply-templates select="descendant::document"/>
    </body>

```

```

        </html>
</xsl:template>
<xsl:template match="document">
    <table frame="hsides" cellpadding="0" align="left">
        <tbody>
            <tr>
                <th width="40%" colspan="2">File Content Labels</th>
                <th width="60%">Study Tagging File<br/>Extract</th>
            </tr>
            <xsl:apply-templates select="doc-content|content-block"/>
        </tbody>
    </table>
</xsl:template>
<xsl:template match="content-block">
    <tr>
        <td colspan="3">
            <font color="blue">
                <xsl:value-of select=".//block-title"/> -- start --</font>
        </td>
    </tr>
    <xsl:if test="property|file-tag">
        <tr>
            <td>
                <td colspan="2">
                    <xsl:apply-templates select="property"/>
                    <xsl:apply-templates select="file-tag"/>
                </td>
            </td>
        </tr>
    </xsl:if>
    <xsl:apply-templates select="doc-content|content-block"/>
    <tr>
        <td colspan="3">
            <font color="blue">
                <xsl:value-of select=".//block-title"/> -- end --</font>
        </td>
    </tr>
</xsl:template>
<xsl:template match="doc-content">
    <xsl:variable name="current-node" select=".//>
    <tr>
        <td valign="top" colspan="2">
            <xsl:apply-templates select="file-tag"/>
        </td>
        <td valign="top">
            <!--This section extracts information from the eCTD backbone file if it is located
            correctly at the sequence folder root-->
            <!--This section creates an xlink pointer to the eCTD backbone leaf through its ID
            attribute value using the STF file's ectd-leaf-id-value as the source for the leaf's ID
            attribute value-->
            Document title=<br/>
            <xsl:value-of select=".//title"/>
            <br/>
            <br/>
            Relative Filename=<br/>
            <xsl:element name="a">
                <xsl:attribute name="href"><xsl:value-of select="@xlink:href"/></xsl:attribute>

```

```

        <xsl:value-of select="@xlink:href"/>
    </xsl:element>
    <br/>
    <br/>
    <xsl:if test=".//property">
        <font color="green">Property=<br/>
            <xsl:apply-templates select="property"/>
        </font>
    </xsl:if>
    </td>
</tr>
</xsl:template>
<xsl:template match="content-block/doc-content">
    <xsl:variable name="current-node" select=".//>
    <tr>
        <td bgcolor="silver" width="2%"/>
        <td valign="top">
            <xsl:apply-templates select="file-tag"/>
        </td>
        <td valign="top">
            <!--This section extracts information from the eCTD backbone file if it is located
            correctly at the sequence folder root-->
            <!--This section creates an xLink pointer to the eCTD backbone leaf through its ID
            attribute value using the STF file's ectd-leaf-id-value as the source for the leaf's ID
            attribute value-->
            <xsl:if test=".//title">
                Document title=<br/>
                <xsl:value-of select=".//title"/>
                <br/>
                <br/>
            </xsl:if>
            Relative Filename=<br/>
            <xsl:element name="a">
                <xsl:attribute name="href"><xsl:value-of select="@xlink:href"/></xsl:attribute>
                <xsl:value-of select="@xlink:href"/>
            </xsl:element>
            <br/>
            <br/>
            <xsl:if test=".//property">
                <font color="green">Property=<br/>
                    <xsl:apply-templates select="property"/>
                </font>
            </xsl:if>
        </td>
    </tr>
</xsl:template>
<xsl:template match="file-tag[@info-type='ich-e3']">
    <!--The next section finds file tags with the info-type value of "ich-e3"-->
    <xsl:value-of select="@name"/>
    <!--The next section confirms that the name value on the file tag is on the ich-e3 list and if
    not, provides a warning-->
    <xsl:choose>
        <xsl:when test="@name=document('')/xsl:stylesheet/internal:vocabulary4leaf-labels-
        file-tag/ich-e3/item"/>
            <xsl:otherwise>
                <br/>

```

```

<font color="red">"<xsl:value-of select="@name"/>" NOT on "<xsl:value-of
select="@info-type"/>" List!</font>
<br/>
</xsl:otherwise>
</xsl:choose>
<!--The next section finds properties with the info-type value of "fda" imbedded in the file
tags (for site identification)-->
<xsl:for-each select="property[@info-type='fda']">
<br/>- <xsl:value-of select="@name"/>...
<xsl:value-of select=". "/>
<!--The next section confirms that the name value on the imbedded property is on the
fda list and if not, provides a warning-->
<xsl:choose>
<xsl:when test="@name=document(/xsl:stylesheet/internal:vocabulary4leaf-
labels-file-tag/fda/fda-site/item)">
<xsl:otherwise>
<br/>
<font color="red">"<xsl:value-of select="@name"/>" NOT on "<xsl:value-of
select="@info-type"/>" List!</font>
</xsl:otherwise>
</xsl:choose>
</xsl:for-each>
<br/>
<br/>
</xsl:template>
<xsl:template match="file-tag[@info-type='fda']">
<!--The next section finds file tags with the info-type value of "fda" (mainly data and
associated files)-->
<xsl:value-of select="@name"/>
<!--The next section confirms that the name value on the file tag is on the fda list and if
not, provides a warning-->
<xsl:choose>
<xsl:when test="@name=document(/xsl:stylesheet/internal:vocabulary4leaf-labels-
file-tag/fda/fda-data/item)">
<xsl:otherwise>
<br/>
<font color="red">"<xsl:value-of select="@name"/>" NOT on "<xsl:value-of
select="@info-type"/>" List!</font>
<br/>
</xsl:otherwise>
</xsl:choose>
<!--The next section finds properties with the info-type value of "fda" imbedded in the file
tags (for site identification)-->
<xsl:for-each select="property[@info-type='fda']">
<br/>- <xsl:value-of select="@name"/>...
<xsl:value-of select=". "/>
<!--The next section confirms that the name value on the file tag is on the fda list and if
not, provides a warning-->
<xsl:choose>
<xsl:when test="@name=document(/xsl:stylesheet/internal:vocabulary4leaf-
labels-file-tag/fda/fda-site/item)">
<xsl:otherwise>
<br/>
<font color="red">"<xsl:value-of select="@name"/>" NOT on "<xsl:value-of
select="@info-type"/>" List!</font>
</xsl:otherwise>

```

```
</xsl:choose>
</xsl:for-each>
<br/>
<br/>
</xsl:template>
<xsl:template match="content-block/property">
<font color="green">
<xsl:value-of select="@name"/>(<xsl:value-of select="@info-type"/>) : <xsl:value-of
select=". "/>
</font>
<br/>
</xsl:template>
<xsl:template match="doc-content/property">
<xsl:value-of select="@name"/>(<xsl:value-of select="@info-type"/>) : <xsl:value-of
select=". "/>
<br/>
</xsl:template>
</xsl:stylesheet>
```